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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/851,628 05/06/97 COHEN

C CRP-145

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HM12/0315

EXAMINER

ROMEO, D

ART UNIT

PAPER NUMBER

1647

DATE MAILED:

03/15/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.  
08/851,628

Applicant(s)  
Cohen et al.

Examiner  
David Romeo

Group Art Unit  
1647



☒ Responsive to communication(s) filed on 9 Nov 2000

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 1-4, 6-10, 12, 15-17, 24, 28, 32, and 52-55 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1-4, 6-10, 12, 15-17, 24, 28, 32, and 52-55 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been  
☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1647

**DETAILED ACTION**

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1647.

5 2. The amendment filed 11/09/2000 (Paper No. 24) has been entered.

3. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

10 Misnumbered claims 33-36 have been renumbered 52-55.

4. Claims 1-4, 6-10, 12, 15-17, 24, 28, 32, 52-55 are pending and being examined.

5. Any objection and/or rejection of record that is not maintained and/or repeated in this Office action is withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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6. Claims 1-4, 6-10, 12, 15-17, 24, 28, 32, 52-55 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application No. 08643321. It is acknowledged that Applicants will file a terminal disclaimer upon the notification of allowable subject matter.

5 **New formal matters, objections, and/or rejections:**

***Claim Rejections - 35 USC § 112***

7. Claims 1-4, 6-10, 12, 15-17, 24, 28, 32, 52-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Support for the limitation "non-immune, non-inflammatory condition" cannot be found in the specification as originally filed and the introduction of such a limitation raises the issue of new matter. Furthermore, the limitation "non-immune, non-inflammatory condition" refers to a subset of renal conditions and the specification lacks written description support for this subset of renal conditions.

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15 8. Claims 1-4, 6-10, 12, 15-17, 24, 28, 32, 52-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of improving renal function or delaying the need for dialysis in a mammal wherein said mammal is afflicted with a

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condition selected from the Markush group in claim 54 or 55, does not reasonably provide enablement for a method of improving renal function or delaying the need for dialysis in a mammal wherein said mammal is afflicted with a non-immune, non-inflammatory condition selected from the Markush group in claim 54 or 55. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are directed to or encompass the treatment of a non-immune, non-inflammatory condition selected from the Markush group in claim 54 or 55. The specification provides the treatment of a 5/6 nephrectomized rat with OP1. However, glomerular and interstitial macrophage accumulation is a feature of most forms of human and experimental glomerulonephritis, and the remnant kidney model is a well characterized rat model of non-immunologically induced renal injury in which there is prominent macrophage accumulation. See Yang (u25)<sup>1</sup>, paragraph bridging pages 1967-1968. Cellular events including glomerular cell proliferation and macrophage influx are associated with increased gene and protein expression by ECM proteins in the remnant kidney model and may contribute to the development of sclerosis. See Floege (v25), Abstract. Furthermore, focal glomerulosclerosis in the remnant kidney model is an inflammatory disease. See Schiller (w25),

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<sup>1</sup>Citations by the examiner are in an alphanumeric format, such as "(a1)", wherein the "a" refers to the reference cited on the Notice of References Cited, PTO-892, and the "1" refers to the Paper No. to which the Notice of References Cited, PTO-892, is attached.

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Title. Although various forms of human and experimental glomerulonephritis may be non-immune, they are not non-inflammatory.

In addition:

5 Klahr (w18) teaches that progressive glomerulosclerosis is typically associated with the infiltration of inflammatory cells and that it is now apparent that these cells may contribute to the progression of renal disease (paragraph bridging pages 1659-1660).

Watanabe (x18) teaches that neutrophilic polymorphonuclear leukocytes are important effector cells in glomerular diseases, including diabetic retinopathy (page 209, column 1, full paragraph 1).

10 Kees-Folts (y18) teaches that close examination of kidneys from patients with a variety of diagnoses has revealed the presence of invading leukocytes in the kidneys of patients with immune and non immune glomerulonephritides (page 366, paragraph bridging columns 1-2). Further, in experimental glomerulonephritides, abrogation of macrophage infiltration results in improved renal function (page 366, column 2, full paragraph 1).

15 Glassock (v6) teaches that monocytes (macrophages) are present in large numbers in the glomerulus and interstitium in many forms of glomerulonephritis and tubulointerstitial nephritis; interference with the accumulation of these cells within the kidney may ameliorate the clinical and morphological manifestations of the disease (paragraph bridging pages 1294-1295).

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Kuberasampath (BB, cited by Applicants) teaches that damage to cells resulting from the effects of an inflammatory response by immune cell mediated tissue destruction has been implicated as the cause of reduced tissue function or loss of tissue function in the kidney; glomerulonephritis is believed to result in large part from unwanted acute inflammatory reactions and fibrosis (page 1, lines 21-33). The immune cell mediated tissue destruction often follows an initial tissue injury or insult; the secondary damage often is the source of significant tissue damage (page 2, lines 7-11). When the interruption of blood flow limits the oxygen supply to the proximal tubular cells of the kidney the cells may become irreversibly injured and the ensuing inflammatory responses to this initial injury provide additional insult to the affected tissue (page 3, full paragraph 1). OP1 (page 14, line 30, through page 15, line 17) inhibits the adherence of LTB<sub>4</sub> activated PMN's to endothelium (Example 5, pages 74-75), inhibits cellular and humoral inflammatory reactions (Example 7, pages 78-80), and inhibits epithelial cell proliferation (Example 10, page 86-87).

The reasonable expectation is that OP1 inhibits the infiltration of inflammatory cells and inhibits the progression of renal disease; OP1 inhibits neutrophilic polymorphonuclear leukocytes as important effector cells in glomerular diseases, including diabetic retinopathy; OP1 abrogates macrophage infiltration resulting in improved renal function; and, OP1 interferes with the accumulation of monocytes (macrophages) within the kidney, thereby ameliorating the clinical and morphological manifestations of renal disease.

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There are no working examples of the treatment of a non-inflammatory condition. The specification lacks guidance for, and working examples of, treatment of non-inflammatory, non-immune renal conditions. The skilled artisan is left to extensive, random, trial and error experimentation in order to determine how to treat a non-inflammatory, non-immune renal condition.

In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

9. The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 are indefinite over the recitation of "non-immune, noninflammatory condition" because it is unclear what type of "non-immune, noninflammatory condition" is intended. It is suggested that the claims recite "non-immune, noninflammatory renal condition".



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*Conclusion*

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

5 A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37  
10 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15 ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 6:45 A.M. TO 3:15 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

OFFICIAL PAPERS FILED BY FAX SHOULD BE DIRECTED TO (703) 308-4242.

20 FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

*David Romeo*  
DAVID ROMEO  
PRIMARY EXAMINER  
ART UNIT 1647

25 MARCH 14, 2001